

REMARKS

Claim 1 has been amended herein. Claims 31-33 were previously cancelled without prejudice. Subsequent to the entry of the present amendment, claims 1-30 are pending and at issue. The amendment adds no new matter, as the claim language is fully supported by the specification and original claims.

I. Rejection under 35 USC § 112, Second Paragraph

Claims 1-7 were rejected under 35 USC § 112 as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action alleges that claim 1 does not recite the step that precedes the administration of the aminosugar. Without acquiescing to the reasoning offered by the Office Action, in order to expedite prosecution towards allowance, Applicants have amended claim 1 herein to read “wherein said treatment comprises administering to said mammal a therapeutically effective amount of an aminosugar,” thereby rendering the rejection moot.

Accordingly, Applicants respectfully request that the rejection under 35 USC § 112, second paragraph be withdrawn.

II. Rejection under 35 USC § 102

Claims 18-19, 22-24 and 27-28 stand rejected under 35 USC §102 as allegedly anticipated by US 5,587,363 (hereinafter, “Henderson”). Applicants respectfully traverse this rejection on the following grounds.

To anticipate a claim, the single prior art reference must disclose each and every element of the claim under consideration. *In re Spada*, 15 USPQ2d 1655 (Fed. Cir. 1990); *Connell v. Sears Roebuck & Co.*, 220 USPQ 193, 198 (Fed. Cir. 1983); MPEP §2131. There must be no difference between the reference disclosure and the claimed invention. *Scripps Clinic & Research Found. v. Genentech, Inc.*, 18 USPQ2d 1001 (Fed. Cir. 1991). Furthermore, the elements must be arranged as required by the claim. *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990).

The Office Action alleges that “Henderson teaches the use of composition comprising glucosamine for the treatment of connective tissue and cartilage repair and arthritis/pain” and “dosages of the aminosugars for the said treatments.” (Office Action, pages 4-5.)

Independent claim 18 recites “[a] method of treating a joint condition comprising the steps of: a. diagnosing a pathological marker associated with a joint condition; and b. administering an aminosugar in a therapeutically effective formulation.” Henderson does not recite the positive step of diagnosing a pathological marker associated with a joint condition, and as Henderson does not teach or suggest this step, the cited reference does not anticipate the invention as claimed. Because Henderson does not anticipate each and every element of the subject claims, the standard for anticipation has not been met.

Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. 102(b) be withdrawn.

III. Rejection under 35 USC § 103

Claims 1-30 stand rejected under 35 U.S.C. §103 as allegedly obvious over Henderson in view of Speck, US 4,870,061 (hereinafter, “Speck”), Nanba, US 5,169,636 (hereinafter, “Nanba”), Burger, US 5,843,919 (hereinafter, “Burger”), Woerly, US 5,863,551 (hereinafter, “Woerly”), Evans, US 6,506,784 (hereinafter, “Evans”), and Wong, WO 00/68194 (hereinafter, “Wong”). This rejection is respectfully traversed on the following grounds.

The U.S. Supreme Court decision in the *KSR International v. Teleflex Inc.* (82 USPQ2d 1385), modified the standard for establishing a *prima facie* case of obviousness. Under the KSR rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

In addition, the U.S. Court of Appeals for the Federal Circuit interpreted *KSR v. Teleflex* (*Id.*) in pertinent part:

In order to find a *prima facie* case of unpatentability ... a showing that the "prior art would have *suggested* making the specific molecular modifications necessary to achieve the claimed invention" was also required. *Id.* (citing *In re Jones*, 958 F.2d 347 (Fed. Cir. 1992); Dillon, 919 F.2d 688; Grabiak, 769 F.2d 729; *In re Lalu*, 747 F.2d 703 (Fed. Cir. 1984)) (*See Takeda v. Alphapharm*, 492 F.3d 1350, Fed. Cir. 2007).

Applicants respectfully submit that the Office Action has not established a *prima facie* case of obviousness.

The pending independent claims as currently amended are:

1. A method of treating a pathology in a mammal, said pathology being selected from the group consisting of synovitis, subchondral bone edema, and cartilage degradation, wherein said treatment comprises administering to said mammal a therapeutically effective amount of an aminosugar, wherein the aminosugar is injected intra-articularly.

9. A method of treating pathologies associated with a joint condition comprising administering a therapeutically effective amount of N-acetylglucosamine as a controlled release formulation.

18. A method of treating a joint condition comprising the steps of:

- a.diagnosing a pathological marker associated with a joint condition; and
- b.administering an aminosugar in a therapeutically effective formulation.

Pending claims are not obvious over Henderson

The Office Action alleges, in pertinent part, that Henderson teaches the use of compositions comprising glucosamine for the treatment of connective tissue and cartilage repair and arthritis/pain. (Office Action, page 6-7) However, a review of Henderson reveals that the cited reference **teaches away** from the present invention. In particular, Henderson states that the use of an aminosugar **alone is ineffective** as a therapeutic composition. (Column 3, lines 19-31.) Henderson recites the "need for a therapeutic composition which include an aminosugar and GAG's (glycosaminoglycans) for aiding in the conversion of these materials to proteoglycans for facilitating the repair of connective tissue in humans and animals" and that the "combination provides the superior connective tissue repair function." (Column 3, lines 27-31; column 7, lines 53-56.) Therefore, one of ordinary skill in the art would not practice Applicants' invention using

the teachings of the cited reference, because one of ordinary skill in the art would not use an aminosugar alone as claimed in the present invention.

Henderson also teaches oral administration of glucosamine, and recites that “[g]lucosamine has been shown to be rapidly and almost completely absorbed into humans and animals after oral administration.” (Column 4, lines 47-54; column 7, lines 36-46.) As such, Henderson does not teach the method of administering a therapeutically effective amount of an aminosugar injected intra-articularly. One of ordinary skill in the art would not administer an aminosugar intra-articularly in view of Henderson.

Therefore, the reference teaches away from the present invention, since the impression left to the skilled artisan is that the ultimate result of practicing the claimed method would not have the property sought by the Applicants. *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 543 (CCPA 1963).

Furthermore, there is nothing in Henderson which discloses or suggests the method of treating a joint condition comprising the steps of: a) diagnosing a pathological marker associated with a joint condition; and b) administering an aminosugar in a therapeutically effective formulation. Applicants submit that because diagnosing a pathological marker associated with a joint condition is clearly necessary as a requisite property of the ultimate product of the method steps, the method of treating a joint condition as claimed in Claim 18 becomes an impossibility.

Therefore, there is no suggestion or motivation to modify Henderson to arrive at the invention as claimed with a reasonable expectation of success. Furthermore, the cited reference does not teach or suggest all of the recited claim limitations. As such, no *prima facie* case for obviousness exists.

Pending claims are not obvious over Speck

The Office Action alleges that Speck suggests the use of N-acetyl glucosamine in combination with excipients via intra-articular injection methods. (Office Action, page 7.)

However, a review of Speck reveals that the cited reference **teaches away** from the present invention of using intra-articular injection. In particular, Speck states that injection of glucosamine is undesirable because an injection preparation is unstable in solution and as such has to be prepared, stored and delivered with an acidic pH-value and has to be neutralized by a

physician before use, and a local anesthetic, such as lidocaine, which can cause adverse side effects, has to be used. (Column 2, lines 15-35.) Speck recites that buccal administration of N-acetylglucosamine solves the problem associated with administration via injection. (Column 3, lines 5-7.) Therefore, one of ordinary skill in the art would not practice Applicants' invention using the teachings of the cited reference, because one of ordinary skill in the art would not administer an aminosugar by intra-articular injection in view of Speck.

Therefore, the reference teaches away from the present invention, since the impression left to the skilled artisan is that the ultimate result of practicing the method would not have the property sought by the Applicants. *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 543 (CCPA 1963).

Furthermore, there is nothing in Speck which discloses or suggests the method of treating a joint condition comprising the steps of: a) diagnosing a pathological marker associated with a joint condition; and b) administering an aminosugar in a therapeutically effective formulation. Applicants submit that because diagnosing a pathological marker associated with a joint condition is clearly necessary as a requisite property of the ultimate product of the method steps, the method of treating a joint condition as claimed in Claim 18 becomes an impossibility.

Therefore, there is no suggestion or motivation to modify Speck to arrive at the invention as claimed with a reasonable expectation of success. Furthermore, the cited reference does not teach or suggest all of the recited claim limitations. As such, no *prima facie* case for obviousness exists.

Pending claims are not obvious over Nanba

The Office Action alleges that Nanba et al. teach compositions comprising oligosaccharides comprising glucosamine and galactosamine residues entrapped by liposomes and that liposomes are models for biological membranes and are effective in stabilizing drugs and achieving sustained release of drugs *in vivo*. (Office Action, pages 7-8) This is incorrect. Nanba recites liposomes which are made up of a liposome lipid membrane containing a glycolipid. (Column 1, lines 66 to column 2, line 16) A glycolipid is a lipid attached to a carbohydrate. A glycolipid is not an aminosugar. Nanba does not disclose or suggest a method

of treating a pathology in a mammal by administering a therapeutically effective amount of an aminosugar, wherein the aminosugar is injected intra-articularly.

Neither does Nanba disclose or suggest the method of treating a joint condition comprising the steps of: a) diagnosing a pathological marker associated with a joint condition; and b) administering an aminosugar in a therapeutically effective formulation. Applicants submit that because diagnosing a pathological marker associated with a joint condition is clearly necessary as a requisite property of the ultimate product of the method steps, the method of treating a joint condition as claimed in Claim 18 becomes an impossibility.

Therefore, there is no suggestion or motivation to modify Nanba to arrive at the invention as claimed with a reasonable expectation of success. Furthermore, the cited reference does not teach or suggest all of the recited claim limitations. As such, no *prima facie* case for obviousness exists.

Pending claims are not obvious over Burger

The Office Action alleges that Burger teaches the treatment of arthritis/osteoarthritis using compositions comprising a combination of glucosamine and N-acetyl glucosamine. (Office Action, page 8.) However, a review of Burger reveals that the cited reference **teaches away** from the present invention. In particular, Burger states that “[l]ittle if any success has been reported in treatment of osteoarthritis...with glucosamine.” (Column 1, lines 53-55.) Burger also recites that “the Arthritis Foundation has stated that it cannot recommend glucosamine as a treatment for any form of arthritis, including osteoarthritis.” (Column 1, lines 61-65.) Burger’s invention discloses the “synergistic activity” which results from “a combination therapy of a glucosamine and an omega-3-fatty acid, which “unexpectedly...has an effectiveness comparable to other presently available medications...without the undesirable side effects.” (Column 2, lines 28-37.) Therefore, one of ordinary skill in the art would not practice Applicants’ invention using the teachings of the cited reference, because one of ordinary skill in the art would not use an aminosugar alone as claimed in the present invention.

Therefore, the reference teaches away from the present invention, since the impression left to the skilled artisan is that the ultimate result of practicing the claimed method would not

have the property sought by the Applicants. *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 543 (CCPA 1963).

Furthermore, there is nothing in Burger which discloses or suggests the method of treating a joint condition comprising the steps of: a) diagnosing a pathological marker associated with a joint condition; and b) administering an aminosugar in a therapeutically effective formulation. Applicants submit that because diagnosing a pathological marker associated with a joint condition is clearly necessary as a requisite property of the ultimate product of the method steps, the method of treating a joint condition as claimed in Claim 18 becomes an impossibility.

Therefore, there is no suggestion or motivation to modify Burger to arrive at the invention as claimed with a reasonable expectation of success. Furthermore, the cited reference does not teach or suggest all of the recited claim limitations. As such, no *prima facie* case for obviousness exists.

Pending claims are not obvious over Woerly

The Office Action alleges in pertinent part that Woerly teaches polymer hydrogels as implants for tissue replacement and regeneration, and that one of skill in the art would recognize the use of the hydrogels for the treatment of degenerative diseases. (Office Action, page 8.) However, a review of Woerly shows that the polymer hydrogels are used to replace or restore missing cells or organs. Nothing in the cited reference discloses nor suggests a method of treating a pathology in a mammal by administering a therapeutically effective amount of an aminosugar, wherein the aminosugar is injected intra-articularly.

Neither does Woerly disclose or suggest the method of treating a joint condition comprising the steps of: a) diagnosing a pathological marker associated with a joint condition; and b) administering an aminosugar in a therapeutically effective formulation. Applicants submit that because diagnosing a pathological marker associated with a joint condition is clearly necessary as a requisite property of the ultimate product of the method steps, the method of treating a joint condition as claimed in Claim 18 becomes an impossibility.

Therefore, there is no suggestion or motivation to modify Woerly to arrive at the invention as claimed with a reasonable expectation of success. Furthermore, the cited reference

does not teach or suggest all of the recited claim limitations. As such, no *prima facie* case for obviousness exists.

Pending claims are not obvious over Evans

The Office Action alleges that Evans teaches a method of treating cartilage degradation using anti-inflammatory agents in combination with glucosamine in different forms and modes of administration for the treatment of articular cartilage degeneration. (Office Action, pages 8-9.) The Office Action also alleges that “[e]ven though Evans teaches the use of glucosamine and anti-inflammatory agents in combination with the compound of formula (I) of his invention, one of skill in the art will recognize that glucosamine and the anti-inflammatory agents alone could be used in the said forms and modes of delivery for the said treatment since the use of glucosamine alone for the treatment of cartilage degradation is taught in the prior art.” Applicants disagree that one of skill in the art would recognize that glucosamine alone could be used. As set forth above, Henderson, Speck and Burger **teach away** from the use of glucosamine alone to treat cartilage degradation. Furthermore, Evans does not teach the use of glucosamine alone, but rather always uses Formula (I) in combination with one or more compounds. Nothing in the cited reference discloses nor suggests a method of treating a pathology in a mammal by administering a therapeutically effective amount of an aminosugar, wherein the aminosugar is injected intra-articularly.

Nor does Evans disclose or suggest the method of treating a joint condition comprising the steps of: a) diagnosing a pathological marker associated with a joint condition; and b) administering an aminosugar in a therapeutically effective formulation. Applicants submit that because diagnosing a pathological marker associated with a joint condition is clearly necessary as a requisite property of the ultimate product of the method steps, the method of treating a joint condition as claimed in Claim 18 becomes an impossibility.

Therefore, there is no suggestion or motivation to modify Evans to arrive at the invention as claimed with a reasonable expectation of success. Furthermore, the cited reference does not teach or suggest all of the recited claim limitations. As such, no *prima facie* case for obviousness exists.

Pending claims are not obvious over Wong

The Office Action alleges that Wong et al. teach that hexoaminidases catalyze cartilage erosion in arthritic subjects from over catabolism of glycosaminoglycans that fill the cartilage tissue and that it would have been obvious to one of ordinary skill in the art to make a formulation comprising amino sugars and use it in a method of treatment as claimed. (Office Action, page 9.) As set forth above, Henderson, Speck, Burger and Evans **teach away** from the use of glucosamine alone to treat cartilage degradation. One of ordinary skill in the art would not use a therapeutically effective amount of an aminosugar, wherein the aminosugar is injected intra-articularly in a method of treatment as presently claimed.

Nor does Wong disclose or suggest the method of treating a joint condition comprising the steps of: a) diagnosing a pathological marker associated with a joint condition; and b) administering an aminosugar in a therapeutically effective formulation. Applicants submit that because diagnosing a pathological marker associated with a joint condition is clearly necessary as a requisite property of the ultimate product of the method steps, the method of treating a joint condition as claimed in Claim 18 becomes an impossibility.

Therefore, there is no suggestion or motivation to modify Wong to arrive at the invention as claimed with a reasonable expectation of success. Furthermore, the cited reference does not teach or suggest all of the recited claim limitations. As such, no *prima facie* case for obviousness exists.

In summary, the cited references do not render Applicants claimed method obvious. None of these references, either alone or in combination, teach or suggest Applicants invention.

The Examiner bears the burden of establishing a *prima facie* case of obviousness. *In re Oetiker*, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). In doing so, the Examiner must determine whether or not the prior art provides the "teaching or suggestion to one of ordinary skill in the art to make the changes that would produce the patentee's" invention. *In re Chu*, 36 USPQ2d 1089, 1094 (Fed. Cir. 1995). In this case, the cited references **teach away** from the use of an aminosugar alone to treat synovitis, subchondral bone edema, and cartilage degradation. As such, the references do not reveal a reasonable expectation of success. *In re Dillon*, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990). Therefore, there is no suggestion or motivation to combine any or

all of the references to arrive at the invention as claimed with a reasonable expectation of success. Additionally, the cited reference does not teach or suggest all of the recited claim limitations.

Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. §103 be withdrawn.

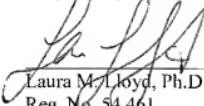
CONCLUSION

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application.

Fees for a two-month extension of time and the fees for a Request for Continuing Examination are submitted herewith. If any additional fees are due, the Commissioner is authorized to charge any fees, or make any credits, to Deposit Account No. 502235 referencing the above-identified attorney docket number.

Respectfully submitted,

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